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Characterization of Tissue Ablation With a Continuous Wave Holmium Laser

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Background and Objective: **The pulsed holmium laser is a promising tool for tissue ablation but possesses some limitations. For example, it is capable of producing significant mechanical damage in certain tissues in the form of fissures and fractures. Because longer pulse durations should reduce mechanical damage, this study examined the tissue effects produced by a prototype continuous wave holmium laser.**
Study Design/Materials and Methods: **A prototype liquid nitrogen cooled holmium operating at 2.12 μm was used. The heat of ablation and ablation threshold were determined using a mass loss technique. Fresh pig skin was irradiated in air or under saline, and prepared for histologic analysis. Hemostasis was qualitatively assessed in vivo during incisions made in the skin, liver, and small intestine.**
Results: **Threshold radiant exposure and heat of ablation were calculated from the mass loss measurements to be 191 J/cm^2 with a 95% confidence interval of −80–440 J/cm^2. Residual thermal damage in skin ranged from 390 to 690 μm in saline and from 390 to 490 μm in air. Excellent hemostasis was achieved in all incisions.**
Conclusion: **Using appropriate irradiation parameters, the continuous wave holmium laser produces tissue effects suitable for a general use surgical instrument. In addition, the laser source could become compact and inexpensive when diode-pumped and direct diode devices become available.**

Key words: laser ablation, thermal damage, mass loss

Introduction

The pulsed holmium laser has attracted considerable attention as a promising general tool for tissue ablation [1]. Because it operates at a wavelength of 2.1 μm, its output is strongly absorbed by water and because it generates pulses brief enough to limit thermal diffusion of the deposited energy, the laser produces residual thermal injury of approximately 500 μm [2]. This degree of residual thermal injury is sufficient to produce small vessel hemostasis. In addition, the laser output is readily transmitted through commercially available optical fibers, making it suitable for endoscopic and laparoscopic use. The use of the pulsed holmium laser has been examined in numerous medical and surgical subspecialties, including cardiology [3], orthopedic surgery [4], urology [5], gynecology [6], otolaryngology [7], and opthalmology [8].

Despite the widespread use of the pulsed holmium laser, there are some limitations of the device. For example, it has been shown that during ablation, a pulsed holmium laser is capable of producing significant mechanical damage in certain tissues in the form of fissures and fractures [9,10]. This is a result of the rapidly expanding and then imploding vapor bubble within the tissue [9]. This

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mechanical damage is undesirable in many clinical applications and may be a limiting factor in the use of the pulsed holmium laser in certain situations. For example, cracks and fissures in blood vessels may enhance thrombogenicity, increase turbulence in blood flow, or produce dissections or ruptures [11]. One method to reduce the mechanical effects is to lengthen the pulse duration [12]. Thus, the use of a continuous wave (cw) holmium laser with laser exposures significantly longer than the conventional pulsed holmium laser should in principle circumvent the limitation of mechanical injury.

Other disadvantages of current commercially available pulsed holmium laser systems are their high cost and large size. Although it is not presently possible to make compact, inexpensive pulsed holmium lasers of adequate power for surgical use, advances have been made in continuous wave holmium technology. Continuous wave diode lasers operating in the wavelength range 1.9–2.1 μm have been demonstrated, and the power of these devices is rapidly increasing. In addition, advances in diode-pumped laser systems operating in the same wavelength range have occurred. Compact, high power diode-pumped devices have been demonstrated by several groups [13]. Both technologies show great promise as surgical devices, but before applications can be developed the tissue effects produced by the cw holmium laser must be examined. In this study, the tissue effects produced by a prototype cw holmium laser system were characterized. A preliminary study comparing cw holmium and cw carbon dioxide lasers has been reported previously [21]. The purpose of the present study was to perform a more detailed study of tissue ablation with a cw holmium laser. Measurements of ablation efficiency, ablation threshold, and residual thermal damage as well as a qualitative assessment of hemostasis were performed.

MATERIALS AND METHODS

Laser

A prototype tungsten lamp excited liquid nitrogen cooled cw holmium:YAG laser (Candela Corp., Wayland, MA), operating at a wavelength of 2.12 μm, was used. The laser could deliver a laser exposure duration between 0.1 and 9 seconds with an output power of up to 20 W. The laser energy was focused by a lens into standard low OH silica fibers.

Mass Loss Experiments

A standard mass loss technique was used [1,2]. The output of the fiber was re-imaged onto the target through a glass lens. A pair of crossed helium-neon laser beams was used to reproducibly locate the target plane. The diameter (full width at half-maximum) of the irradiated area was measured by translating a 320 μm core-diameter quartz fiber across the beam and measuring the transmitted laser energy with a standard laser energy meter.

Fresh chicken liver was used as the target. Samples were formed with a 6 mm punch biopsy needle and immediately mounted in a sample holder. The small sample size was used to minimize evaporative loss. The mass of the target was measured by an analytic balance with a precision of 10 μm (model AE163, Mettler Instrument Corp., Hightstown, NJ). A personal computer sampled the digital output of the balance at a rate of 2.4 samples/sec and stored the data for further analysis.

Residual Thermal Damage

Samples of porcine skin were obtained by removing the full thickness of skin from a pig immediately post mortem. The skin samples were mounted on paraffin blocks immediately and kept moist by wrapping the samples in saline moistened gauze. Multiple sites on the skin were irradiated by placing the output fiber from the laser in gentle, perpendicular contact with the tissue. Measurements were made with the samples in air or immersed in saline. After irradiation, the tissue was fixed in 10% formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin.

Hemostasis

In order to qualitatively assess hemostasis, a young farm pig was placed under general anesthesia using inhaled halothane. After adequate anesthesia was obtained, multiple incisions in skin, liver, and small intestine were made using the cw holmium laser delivered through a 400 μm core diameter quartz fiber in the noncontact mode. The degree of hemostasis was judged qualitatively by the surgeon.

RESULTS

Mass Loss Experiments

The diameter of the laser spot on the surface of the target was measured to be 750 μm. The

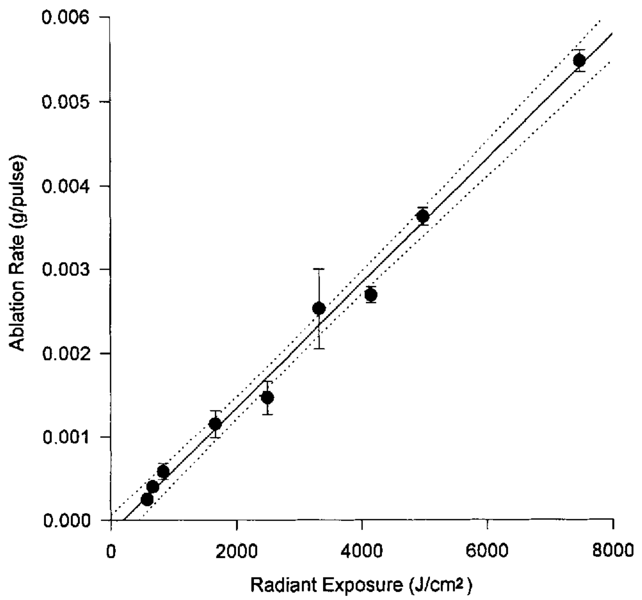

Fig. 1. Ablation rates determined from mass loss measurements are plotted as function of radiant exposure. The linear least squares fit to the data is shown as a solid line; the dotted lines represent the 95% confidence intervals for the mean ablation rates.

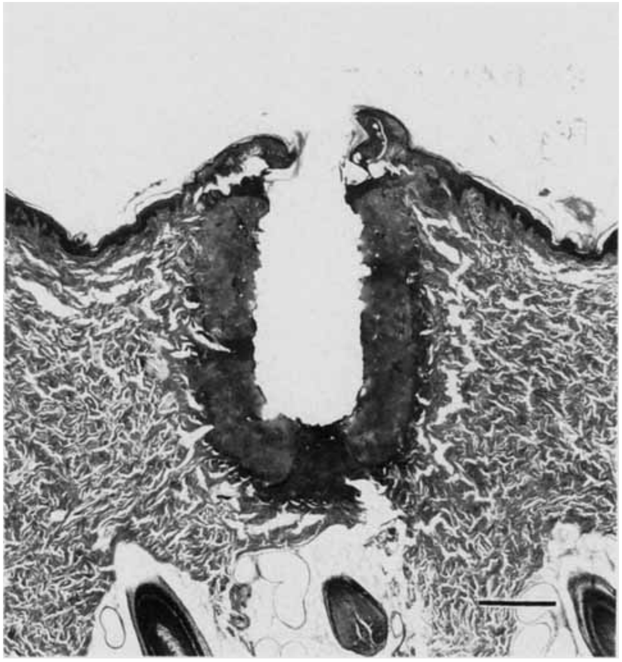

Fig. 2. Photomicrograph of an ablation crater produced in pig skin under saline. Laser parameters: power 10 W, exposure duration 0.3 s, fiber core diameter 600 μm. The bar corresponds to 400 μm.

laser output power was fixed at 3.67 W, and the delivered radiant exposure was varied by varying the laser exposure duration in the range 0.1–9 s. Mass loss was measured during the delivery of the laser energy from a single exposure.

Figure 1 shows the effect of radiant exposure on mass loss. Mass loss increased linearly with radiant exposure. The best fit slope resulting from a linear least squares fit was 0.744 μg-cm^2/J. The best fit slope was then divided by the irradiated area (0.00442 cm^2) to yield an equivalent slope of 168 μg/J. If the density of liver is assumed to be 1.1g/cm^3, the slope can be converted to a heat of ablation of 6,500 kJ/cm^3.

The threshold radiant exposure for ablation was taken to be the radiant exposure at which the linear regression line estimated an ablation rate of zero. The threshold was estimated to be 191 J/cm^2 with a 95% confidence interval (−80–440 J/cm^2).

Residual Thermal Damage

The effect of varying laser exposure duration, output power, and fiber diameter on residual thermal damage was assessed. The zone of residual thermal damage was determined by light microscopy and taken to be the region of tinctorial and polarization change as shown in Figure 2. The depth of this altered zone below the base and along the crater walls was measured for each irradiation site and averaged. The experimental results are summarized in Table 1. Residual thermal damage increased with laser exposure duration when the tissue was ablated in saline but was constant when ablated in air.

Hemostasis

In skin, no bleeding was observed during the production of linear incisions. There was also no bleeding from laser incisions in the liver and small intestine. This was qualitatively compared with adjacent scalpel cuts in which profuse bleeding was observed from the liver.

DISCUSSION

The purpose of this study was to characterize the tissue effects produced by a cw holmium laser. The study demonstrates that cw holmium laser transmitted through low OH silica optical fibers can ablate tissue with submillimeter zones of thermal injury adjacent to ablation sites in saline as well as in air. Quantitative measurements of ablation show that once a threshold radiant expo-

TABLE 1. Residual Thermal Damage

Spot size (μm)	Power (W)	Exposure (s)	Environment	Thermal damage (μm)
600	10	0.1	Air	472 ± 41
600	10	0.2	Air	390 ± 41
600	10	0.3	Air	488 ± 143
600	10	0.5	Air	421 ± 20
600	10	0.7	Air	429 ± 84
600	10	0.1	Saline	443 ± 24
600	10	0.2	Saline	386 ± 46
600	10	0.3	Saline	368 ± 60
600	10	0.5	Saline	434 ± 47
600	10	0.7	Saline	562 ± 187
600	10	1.0	Saline	536 ± 54
600	10	1.5	Saline	386 ± 83
350	5	0.2	Air	484 ± 64
350	5	0.3	Air	444 ± 34
350	5	1	Air	479 ± 86
350	5	0.2	Saline	354 ± 30
350	5	0.3	Saline	450 ± 37
350	5	0.5	Saline	513 ± 65
350	5	1.5	Saline	691 ± 135

Values of thermal damage are tabulated as the mean ± 1 SD.

sure is exceeded, ablation rate is directly proportional to the delivered radiant exposure.

When modeling laser ablation, an energy balance approach is widely used [14]. In this model, the ablation rate is expressed as

$$R = A\rho(F - F_{th})/H, \tag{1}$$

where R is the ablation rate expressed as mass ablated per pulse, ρ is the density of the target, A is the area irradiated by the laser, F is the delivered radiant exposure per pulse, F_{th} is the threshold radiant exposure, and H is the heat of ablation. Using this model, the heat of ablation was calculated to be 6.5 kJ/cm^3. Because the tissue was irradiated with exposures longer than the tissue thermal relaxation time, as discussed later, some energy was likely lost to diffusion, making the energy density actually used to ablate tissue somewhat lower than 6.5 kJ/cm^3.

The threshold radiant exposure determined in this study was 191 J/cm^2. This value is somewhat larger than the 20 J/cm^2 obtained previously with pulsed holmium lasers [15]. Because of the wide confidence interval for the threshold radiant exposure in this study, it is uncertain whether there is an actual difference in threshold between the two lasers. However, the thresholds for pulsed irradiation might be less than for cw irradiation because of energy losses due to heat diffusion as well as inertial confinement effects [15,16]. In our experiments the laser pulse duration was longer than the pressure relaxation time t_d given by

$$t_d = 1/\alpha c_s, \tag{2}$$

where t_d is the pressure relaxation time, α is the optical absorption coefficient (24 cm^{-1}), and c_s is the speed of sound in water (1,430 m/s). Using these values results in a pressure relaxation time of 0.3 μs. For pulse durations longer than the pressure relaxation time, the pressure rise is diminished due to mechanical relaxation, and this might result in an increased ablation threshold [15,16].

Pulse duration is an important parameter in determining ablation efficiency, the extent of mechanical damage, and the extent of residual thermal injury. If the pulse duration exceeds the time required for a significant amount of heat to diffuse from the ablation site, thermal injury will occur outside the volume of tissue initially heated by the laser. Thus, one popular technique to minimize residual thermal damage is to use laser pulse durations shorter than the thermal relaxation time of the target [17]. Because the optical penetration depth and laser beam diameter are of comparable magnitude, the relevant relaxation time in this case is a combination of radial and axial diffusion times. This thermal relaxation can be estimated using heat transfer theory [2]:

$$1/t = 4\kappa(\alpha^2 + 1/r^2), \tag{3}$$

where t is the thermal relaxation time, α is the tissue absorption coefficient at the laser wavelength (24 cm^{-1}), κ is the thermal diffusivity of the target, and r is the radius of the irradiated area.

If it is assumed that the thermal diffusivity of tissue is 0.0013 cm^2/s [18], equation (3) yields estimated thermal relaxation times of 114 ms and 43 ms for spot diameters of 600 μm and 320 μm, respectively.

In this study, laser exposure durations were varied from 100 ms to 1,500 ms, which span the estimated thermal relaxation times. The experiments revealed that residual thermal damage in pig skin was not sensitive to laser exposure duration in the range 100–1,000 ms when irradiated in air. The residual thermal damage obtained under these conditions was comparable to those obtained with a pulsed (250 μs) holmium laser in guinea pig skin in air [2]. An interesting trend in

thermal damage as a function of laser exposure duration was noted for a laser spot diameter of 350 μm when the irradiation occurred in saline. For example, the residual thermal damage for an exposure time of 0.2 s was significantly smaller than for an exposure duration of 1.5 s ($P < 0.025$, *t*-test).

No statistical differences between the mean measured residual thermal damages were seen for irradiations in air. This suggests that residual thermal damage may increase at longer exposure durations under these specific conditions. For the larger spot size studied, this trend was not as prominent, although the mean residual thermal damage between exposure times of 0.1 and 1.0 s but not 1.5 s were statistically different ($P < 0.025$, t-test). Thus, a trend toward increasing thermal damage might be present for this spot size as well. Further studies will be needed to establish the validity of this hypothesis. The reason for this dependence upon the saline environment, if it indeed occurs, is not entirely clear but may be the result of heat removal from the tissue surface by saline. Heat removal from the surface impedes the ablation process and may allow heat to penetrate deeper into the tissue, producing thermal injury at greater depths [19].

Although these experiments were not designed to examine the effects of acoustic/stress waves on tissue, no gross fractures of tissue were seen. Also, violent ejection of material from the surface of the ablation site was not observed, as has been noted with pulsed holmium lasers. From the standpoint of acoustic injury at the cellular level, it has been shown that stress transients greater than 30 bar/ns produce acoustic injury to EMT-6 cells [20]. Although we did not directly measure the stress transients generated by the cw laser, the irradiation conditions are well below those expected to produce such high stresses.

In summary, a cw holmium laser can effectively ablate tissue with ablation rates that increase linearly with delivered energy. The zone of residual thermal damage was comparable with that produced by a pulsed laser. In addition, excellent hemostasis was observed and no evidence of mechanical injury was noted.

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